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THE COURSE OF IRON DEFICIENCY ANEMIA IN CHILDREN CURRENT AND FORECAST FOR THE FUTURE

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Annotation: The article presents data on the incidence, etiology, pathogenesis and clinical manifestations of iron deficiency anemia(IDA), principles of diagnosis and treatment of the disease in children and adolescents. The article presents the most frequently used iron preparations for oral therapy, intramuscular and intravenous administration in Uzbekistan, their advantages and disadvantages, as well as the principles of monitoring the effectiveness of treatment. Various types of prevention are described: at the population level (fortification), in groups at risk of IDA development (complementing), primary and secondary prevention. Recommendations of the American Academy of Pediatrics on the prevention of IDA in the most vulnerable group of the population — infants and young children-are presented.

Keywords: children, adolescents, iron deficiency anemia, diagnosis, treatment, iron preparations, prevention.

Iron deficiency anemia (IDA) is an acquired disease from the grou p of deficient anemia; it is accompanied by microcytic, hypochromic, normo regenerative anemia; it is clinically manifested by a combination of sideropenic and anemic syndromes. IDA includes the following nosological forms that have the corresponding codes for the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10): IDA (D50), chronic posthemorrhagic anemia (D50. 0), anemia that complicates pregnancy, childbirth and the postpartum period (O99. 0). In childhood, IDA accounts for 90% of all anemia. It occurs in all countries of the world, but its prevalence depends on socio-economic conditions, income of the population, the nature of nutrition and other factors. Infants and young children, adolescents, women of childbearing age, pregnant and lactating women are at the greatest risk of developing IDA [1]. The prevalence of anemia in its diagnosis by low hemoglobin (Hb) concentration in various age groups in developed and developing countries is presented. According to WHO experts, if IDA is detected in more than 40% of the population, the problem ceases to be medical and requires a decision at the state level [1]. Etiology of IDA The main cause of iron deficiency in the human body, according to WHO experts, is improper (inadequate) nutrition. Much less often, IDA develops as a result of helminthic infestations or as a result of chronic post-hemorrhagic anemia. The main causes of IDA development in children and adolescents are: iron deficiency at birth (fetoplacental transfusion); alimentaryiron deficiency due to inadequate nutrition; increased body needs for iron (pid growth of a child aged 1-3 and 14-16 years, professional sports, pregnancy); loss of iron and body weight higher than normal (bleeding of various etiologies, including heavy menstrual blood loss, postpartum anemia). Alimentary-dependent factors in the development of iron deficiency in children are [2]: insufficientiron intake with food (excluding breastfeeding at the age of 4 months, late introduction of complementary foods, unbalanced nutrition, vegetarianism); reduced iron absorption; increased iron loss. The causes of chronic post-hemorrhagic anemia in men can be various diseases of the gastrointestinal tract — gastrointestinal tract (ulcerative bleeding, colon polyps, ulcerative colitis, intestinal angiomatosis, Meckel diverticula, hemorrhoid bleeding, stomach and intestinal tumors); in women, in the structure of the causes of chronic post-hemorrhagic anemia,

uterine bleeding is in the first place. and diseases of the gastrointestinal tract occupy the second place. Pathogenesis of IDA is a group of anemic conditions of various etiologies, the main pathogenetic is ropenia). As a result of iron deficiency in the body, Hb synthesis is disrupted and its content in red blood cells decreases. The number of red blood cells may also decrease slightly. Since the red blood cell count and Hb content decrease unevenly, red blood cell hypochromia develops, which reflects a reduced color index (CP). Violation of Hb formation leads to a decrease in red blood cell indices — the average volume of the red blood cell (MCV) and the content of Hb in the red blood cell (MCH). Anisocytosis becomes pronounced (due to the predominance of small red blood cells). In the bone marrow, erythroid hyperplasia is detected with a predominance of polychromatophilic or oxyphilic normoblasts. The number of erythroid cells containing hemosiderin decreases sharply. Depletion of iron reserves leads to a disorder of redox reactions in tissues, which causes damage to the skin, mucous membranes, gastrointestinal tract dysfunction, and a decrease in the activity of many iron-containing enzymes. Clinical manifestations The development of IDA is preceded by latent iron deficiency, which does not have an independent ICD-10 code, but is characterized by the presence of sideropenic syndrome. The clinical manifestations of IDA are a combination of two syndromes-sideropenic According to the degree of absorption and safety profile of oral iron divalent drugs, iron gluconate preparations are optimal. Properties and advantages of iron preparations based on the hydroxide-polymaltose complex of trivalent iron: high efficiency; high safety, no risk of overdose, intoxication and poisoning; no darkening gums and teeth; pleasant taste; excellenttolerance (high compliance); excellent interaction with other medicines and food;no antioxidant properties. If there is a latent iron deficiency, half-dose oral iron supplements and fortifying supplements may be prescribed. Parenteral (intravenous and intramuscular) iron preparations are indicated in cases where oral medications cannot be used or they are ineffective. Parenteral iron preparations in the treatment of IDA are indicated for: severe IDA (currently quite rare — about 3% of cases); intolerance to oral iron preparations; resistance to treatment with oraliron preparations; presence of gastrointestinal ulceror duodena ulcer or gastrointestinal surgery, even in the anamnesis; anemia, diseases associated with chronic bowel diseases (ulcerative colitis, Crohn's disease); chronic kidney disease for the treatment and prevention of anemia during predialysis and dialysis periods; auto-donation before surgery; presence of contraindications to pored blood mass transfusions, including those based on religious beliefs (for example, Jehovah's Witnesses); the need and rapid saturation of the body with iron. Some modern iron preparations for parenteral administration are given in Table. 6. Intramuscular or intravenous iron injections are usually given 2-3 times a week. When using parenteral iron supplements, it is not recommended to exceed the total iron deficiency. Number of ampoules to be administered = Total Iron deficiency 100 mg Adverse events when using parenteral iron preparations, Both methods of administration (intravenous and intramuscular) can cause various adverse events — local (redness, burning, itching) and general (allergic, anaphylactoid). The latter are typical for parenteral iron preparations containing dextran. This requires monitoring the patient, applying a test dose before starting treatment, and accurately calculating the amount of iron that should be administered to avoid the damaging effect of its increased concentration in the circulation. It is necessary to keep in mind the possibility of adverse events due to the patient's hypersensitivity to iron preparations administered even in very low doses. In order for parenteral iron therapy to be effective and safe for the patient, the following treatment principles must be strictly followed: the use of modern parenteral iron preparations with lower toxicity, without life-threatening anaphylactoid reactions; determination of the totaliron deficiency in the patient's body according to the formula indicated above; discontinuation of therapy after replenishment of the patient's body. general iron deficiency in order to avoid dangerous over-saturation of the body with iron. For the same reasons, it is advisable to conduct parenteral iron therapy under the control of transferrin saturation with iron; compliance with the technique of intra muscular injection and intravenous infusion of iron preparations; mandatorycompliance with the instructions for use of parenteral iron preparations, if a trial dose is provided before starting treatment; treatment isrecommended to be carried out in the safe dose range, since adverse events of parenteral iron preparations are dose-dependent. Red blood cell mass transfusion In IDA, as a rule, there are no indications for red blood cell mass transfusion. Even severe cases of IDA can be successfully treated

with oral, intramuscular, or intravenous iron supplements. The risk of using red blood cell mass transfusions in the treatment of IDA clearly exceeds the benefit from them. Complications of treatment The use of iron salts may be accompanied by complications in the form of gastrointestinal toxicity with the development of symptoms such as epigastric pain, constipation, diarrhea, nausea, vomiting. This leads to low compliance of IDA treatment with saline iron preparations — 30-35% of patients who started treatment refuse to continue it. Possible overdose and even poisoning with saline iron preparations due to passive uncontrolled absorption. Modern iron preparations based on the hydroxide-polymaltose complex of trivalent iron (Maltofer, Ferrum Lek) do not cause such complications and are well tolerated. Monitoring the effectiveness of treatment of the disease the effectiveness of IDA treatment depends on the proper nutrition of the patient, the dose of iron preparations, the duration and implementation of the entire course of treatment, and the elimination of the source of blood loss in the case of chronic post-hemorrhagic anemia. Monitoring of the response to treatment with iron preparations can be performed by: reticulocytico reaction: an increase (by 1-2% or 10-20 % compared to the initial one) in the number of reticulocytes on days 7-10 from the start of treatment indicates the correct diagnosis of IDA and early effectiveness of treatment with iron preparations; fixed response criteria, for example, once developed (The US Centers for Disease Control (CDC for Disease Control), according to which by the end of the 4th week of IDA treatment with iron preparations, the concentration of Hb should increase by 10 g/l, and Ht — by 3% compared to their initial values [14]. The cure for IDA is considered to be the elimination of tissue sideropenia and the restoration of iron reserves, and not just the achievement of normal Hb concentrations. This should be proved by normalizing the concentration of serum ferritin [15] (if possible). If this option is not available, it is necessary to follow the standard terms of treatment for IDA, depending on the severity of anemia (from 3 to 6 months). Prognosis of the disease The prognosis of the disease is favorable: cure occurs in the vast majority of cases. So-called" relapses " of the disease are possible: with the use of low doses of iron preparations; ineffectiveness of oraliron preparations, which is rare; reductionand duration of treatment of patients; treatment of chronic post-hemorrhagic anemia with an undetected or non-eliminated source of blood loss. Very rarely, a cure with the help of standard therapy with iron preparations can not be achieved. American scientists have found that the poor response to iron therapy in IDA is due to the presence of a mutation in the TMPRSS6 gene, which leads to excessive production of hepcidin, which blocks the absorption of iron in the intestine and prevents its release from macrophages [16]. That is why anemia in such patients does not respond to treatment with either oral or intravenous iron preparations. Dispensary monitoring of IDA patients Dispensary monitoring of children and adolescents with IDA is carried out within one year from the moment of diagnosis. The patient's state of health and general condition are monitored. Before removing the patient from dispensary observation, a clinical blood test is performed, all indicators of which should be within the normal range. Vaccination Preventive vaccinations in children with IDA are not contraindicated, do not require normalization of Hb, and should be carried out within the usual time frame. Rehabilitation measures Medical, physical and psychological rehabilitation of patients after recovery from IDA is not required. Prevention measures If the prevalence of IDA in a country or region exceeds 40%, WHO experts recommend fortification, which involves fortifying the most commonly consumed foods with iron. Usually, bread or pasta is chosen as such products. It is important that the proportion of the population using this product is at least 65-95%. Fortification is difficult due to the lack of an ideal food product that would combine well with iron, as well as problems with its absorption. The efficiency of fortification is about 50% among the population covered. Prevention of IDA in populations at risk for anemia is considered more effective. This type of prevention is called saplimentation and involves the addition of substances (iron, iodine, etc.) from the outside [17]. The most significant example of complimentation is the use of iron preparations in pregnant women for the prevention of IDA. According to WHO recommendations, the iron preparation at a dose of 60 mg / kg per day is used in the second and third trimesters of pregnancy and during 3 months of lactation. US national guidelines provide for the use of iron preparation at a dose of 30 mg / kg per day during the entire period of pregnancy. Even with 50%, 80%, and 95% of pregnant women receiving supplementation, only 67% of women receive an effective dose of iron. Unfortunately, such

recommendations have not been developed in our country. Primary prevention of iron deficiency The problem of iron deficiency is primarily a problem of nutrition, so primary prevention of IDA is an adequate, balanced diet of a person at any age. The daily requirement of an adult for iron is about 1-2 mg, a child-0.5-1.2 mg. The usual diet provides from 5 to 15 mg of elemental iron per day. In the gastrointestinal tract (duodenum and upper jejunum), only 10-15% of the iron contained in food is absorbed. The main food source of iron is animal products containing heme iron. The greatest amount of iron is found in beef, lamb, liver; to a lesser extent — in fish, chicken meat, cottage cheese. The important thing is not how much iron is contained in the product, but what is its bioavailability. Compared to animal products, non-heme iron contained in plant foods (vegetables, fruits, cereals) has a reduced bioavailability, which means its lower absorption. In addition, certain conditions are necessary for the absorption of iron: vitamin C increases the absorption of iron, and substances such as tannic acid, which is part of tea, or phytates found in some products, can significantly inhibit the absorption of iron. In IDA, iron absorption in the duodenum increases dramatically, which is associated with suppression of hepcidin synthesis. Currently, most countries around the world have adopted appropriate recommendations for the prevention of iron deficiency. They mainly concern young children, pregnant and lactating women, as well as women of reproductive age American Academy In 2010, the American Academy of Pediatricsrevised its recommendations for the prevention of IDA in infants and young children (1-3 years of age). The main provisions of these recommendations are as follows [18]: full-term healthy children have sufficient iron reserves in the first 4 months lives. Due to the low iron content in breast milk, children who are breastfed are shown to be additionally prescribed iron (1 mg of iron per 1 kg of body weight per day), starting from 4 months of age and before the introduction of complementary foods (for example, porridge enriched with iron); full-term children who are on mixed feeding (breast milk makes up more than half of the diet), should receive an additional 1 mg of iron per 1 kg of body weight per day, starting from the age of 4 months and up to complementary feeding; children who are on artificial feeding and receive iron-rich milk formulas receive a sufficient amount of iron from milk formulas or complementary foods. Whole cow's milk should not be given to children under 12 months of age; children aged 6-12 months should receive 11 mg of iron per day. As complementary foods, red meat and vegetables with a high iron content should be prescribed. In case of insufficient intake of iron with formula or complementary foods, iron should be additionally prescribed in the form of drops or syrup; children aged 1-3 years should receive 7 mg of jellyper day, preferably in the form of food containing sufficient amounts of red meat, vegetables with a high iron content and fruits with a high content of vitamin C, which increases the iron absorption. Additional supplementation of liquid forms of iron supplements or multivitamins is also possible; all infants born prematurely should receive at least 2 mg of iron per 1 kg of body weight per day up to 12 months of age, which corresponds to the iron content of fortified infant formulas. Infants born prematurely should be breastfed with 2 mg of iron per 1 kg of body weight per day, starting from the 1st month of life and until the transition to artificial feeding with iron-enriched milk formulas, or until the introduction of complementary foods that provide 2 mg of iron per 1 kg of body weight per day. In case of detection of risk factors for IDA in young children, it is recommended to conduct selective screening at any time [18]. Children aged 2-5 years who do not have risk factors are screened for IDA annually. Among school-age children and adolescent boys, children with a history of IDA or special needs due to health conditions or low dietary iron intake should be screened for anemia. Starting in adolescence, screening for anemia is performed in all nonpregnant women every 5-10 years throughout childbearing age. Women with risk factors for IDA (heavy blood loss during menstruation or otherwise, insufficient iron intake, and a previous diagnosis of IDA) should be screened annually. Taking iron supplements for preventive purposes is intended for people from risk groups who do not have the opportunity to receive iron-rich foods. It should be remembered that iron from fortified foods is included in erythropoiesis to a lesser extent than when prescribing iron preparations. Unfortunately, Russian scientists have not yet formulated such scientifically based recommendations for the prevention of iron deficiency in various population groups. The development of national recommendations for the prevention and treatment of iron

deficiency conditions and their approval at the state level will solve a complex medical and social problem.

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